

Metabolic Disorders Cardiac: Disturbances Triggers by Lack of ATP?

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Abstract

Occidental lifestyle including lack of physical activity, are related to risk of developing heart diseases. ATP has a central role in understanding cardiac metabolism. Thus, this study was carried out to discuss aerobic cardiac metabolism, with most of the energy provided by oxidative phosphorylation. The ATP produced by this pathway is essentially used for contraction in non-pathological conditions. In addition, situations are discussed on the glycolytic pathway to produce ATP under pathological conditions. Thus, in some cardiomyopathies, the manipulation of the metabolic status of the heart represents an attractive alternative for the prevention of later complications.

Keywords: Myocardium; Myocardium diseases; Metabolism

Introduction

Worldwide, cardiovascular diseases are the main cause of death in the occidental lifestyle [1]. In the countries of America, 75% of deaths are associated with heart diseases [2,3].

The risk of developing heart diseases can be explained by side-reactions of the metabolism, which has been shown to promote oxidative stress through the elevated reactive oxygen species (ROS) production and/or reduced antioxidant defense which causes the decrease of health and well-being of biological systems and their functions [3-5].

Normal cardiac function depends on the adequate supply of oxygen and oxidizable substrates to generate sufficient adenosine triphosphate (ATP) to elicit the demand of the heart. This method is stuck through chemical methods of metabolism, including glycolysis, which directly participates in the generation of ATP. Research on the mechanisms that lead to cardiovascular diseases have mainly focused on the study of mechanical factors (overload, muscle tone) and chronotropic agents involved [6,7]. However, the role of energy metabolism in the onset and development of heart disease is poorly understood, although some articles describe metabolic changes or use of metabolic support, but did not show a cause and effect relationship between metabolism and cardiovascular disease. In addition, it is important to identify how we can contribute to understanding the heart disease [7,8].

Energy Substrates in the Heart

Cardiac metabolism is predominantly aerobic, with most of the energy supplied by oxidative phosphorylation. The ATP produced by this pathway is essentially used for contraction [3,7-9].

Heart preferentially oxidizes the fatty acids under normal conditions [9-12]. According to Montini et al. from 5 mM glucose 0.1 mM to 0.4 mM palmitate lactate, the relative contribution to ATP formation in isolated cardiac myocytes is 26, 34 and 40%, respectively. The increase in lactate concentration to 7.5 mM (simulating increased skeletal muscle activity of the body) results in a greater and predominant contribution of lactate oxidation to the ATP supply of approximately 64% [13]. Availability of substrates to the myocardium may vary depending on several factors, such as the nutritional status of the individual. Thus, during starvation, the energy demand in the heart is provided by ketone bodies (78%) and fatty acid oxidation (22%) [2,5,7]. This change in substrate preference results from a large increase in the plasma concentration of ketone bodies (from 0.19 to 4 mM for hydroxybutyrate and from 0.17 to 1.2 mM for acetoacetate), increase in fatty acids (from 0.35 to 0.82 mM for palmitate) [2-7,14].

Variations in Glucose Oxidation

It is well-described glycolysis to supply of ATP in adult heart is small. However, there is evidence that glycolytic pathway greatly contributes to ionic gradients used for depolarization during myocyte excitation, in addition to maintenance of K^+ and Na^+ homeostasis [3,7,9,10,11,14]. During the acute increase in effort, glucose oxidation also provides important levels of ATP to cover the high energy demand [3,8].

It described relationships between changes in the glycolytic pathway and some heart disease. In a diabetic animal model there is a decrease in the transport of glucose from the blood to the myocardial cell. In fact, GLUT-1 and GLUT-4 protein levels decrease in diabetes, but may be normalized by physical exercise or by treatment with insulin [3,4,10,11,15]. In addition to altered glucose transport, diminished oxidation of this substrate has been observed.

A similar effect was found in an experimental model of hypertriglyceridemia developed by our group, in which the low cardiac mechanical performance correlated with low levels of active Pyruvate dehydrogenase [10-15]. On the other hand, Carvajal and Baños [7] explain in diabetic animals with low susceptibility to the development of hypertriglyceridemia are resistant to the development of cardiomyopathy.

Diets rich in carbohydrates induce stimulation of fatty acid synthesis and the onset of hypertriglyceridemia [3,5,7]. In the diabetic pig heart that develops low cardiac work, the stimulation to increase work - which supposedly accelerates the oxidation of pyruvate [7-9].

These data suggest derangement of mitochondrial carbohydrate metabolism in diabetic myocardium. Lack of Pyruvate dehydrogenase response to work load or electrical stimulation also is evident in sugar-induced hypertriglyceridemic rat heart [7,9-11].

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Conclusion

The majority of heart disease in which it presents mechanical dysfunction is associated with disorders in one or more metabolic stages of the ATP production pathways. In some cardiomyopathies the manipulation of the metabolic status of the heart represents an attractive alternative to therapy and, in general, to prevention of further complications.

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